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Effects of Verapamil and Lidocaine in a Canine Model of Sudden Coronary Death

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The efficacy of verapamil and lidocaine for treating ischemia-induced arrhythmias was determined in a conscious canine model with a previous myocardial infarction remote from the ischemic area. Temporary (up to 5.5 minutes) occlusion of the circumflex coronary artery was made in eight conscious dogs that had sustained an anterior myocardial infarction 13 to 35 days previously. Each dog served as its own control. Ventricular arrhythmias were observed in 100% of control experiments but in only 25% of experiments after verapamil pretreatment at 0.4 mg/kg body weight. Repetitive ventricular complexes, defined as two or more consecutive ventricular complexes terminating spontaneously in sinus rhythm, were seen in 88% of control experiments and 13% of verapamil experiments, whereas ventricular fibrillation was seen in 6% of control experiments but in no verapamil experiment. Thus, verapamil abolished arrhythmias or reduced the grade of arrhythmias in all dogs.

Six of the eight dogs were also tested with lidocaine pretreatment at one or two doses resulting in mean plasma levels of 3.8 ± 2.0 μg/ml. Ventricular arrhythmias were seen in 92% of control experiments and 100% of lidocaine experiments. The incidence of ventricular fibrillation increased from 8% in control to 60% in lidocaine experiments. It is concluded that verapamil may prevent severe ischemia-induced arrhythmias after a recent myocardial infarction, whereas lidocaine may in some cases aggravate arrhythmias.

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Clinical studies of patients with cardiac arrest who were resuscitated out-of-hospital and who have acute myocardial infarction have suggested that ventricular fibrillation frequently occurs within a few minutes after coronary flow is compromised (1–4). The abruptness with which such arrhythmia strikes makes it particularly difficult to perform clinical studies. Although there are clinical data from patients with a previous myocardial infarction indicating that prophylactic beta-adrenergic blocking agents are effective in reducing the incidence of subsequent death, the utility of other prophylactic pharmacologic interventions including therapy with the traditional antiarrhythmic agents that block the so-called fast sodium channel remains unproven (5,6).

The purpose of this study is to compare pretreatment with a slow (calcium) channel blocker, verapamil, with pretreatment with a fast (sodium) channel blocker, lidocaine, in a conscious canine model of sudden coronary death due to coronary occlusion in a heart with a previous myocardial infarction.

The ischemia-induced arrhythmias observed within minutes of occlusion in animal models are thought to be analogous to these lethal clinical arrhythmias (7–9). Previous studies (10–13) in animal models have shown that verapamil pretreatment has a protective effect against ventricular arrhythmias produced by ischemia. Pretreatment with lidocaine has not been consistently demonstrated to be beneficial (14–17). However, these observations were made on ventricular arrhythmias after abrupt coronary occlusion in open chest animals and these are influenced by altered sympathetic tone and by the effects of anesthesia. Because altered sympathetic tone and anesthesia may affect these arrhythmias, it is important to confirm such data in a conscious animal model more analogous to the clinical state (18–20). The present model also differs from previous models in that ischemia is produced in the presence of a previous myocardial infarction.

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Methods

Experimental model. Twenty-two adult mongrel dogs of both sexes weighing 18 to 22 kg were selected on the basis of apparent good health and reasonable disposition. They were anesthetized intravenously with sodium pentobarbital, 30 mg/kg body weight. Using sterile surgical technique, the thorax was opened through the fourth left intercostal space. A balloon occluder developed by Barger (Hazen Everett Co.) was placed around the proximal left circumflex coronary artery. An acrylic plaque, 5 × 7 × 2 mm, containing five silver contacts was sutured to the left ventricular epicardium in the distribution of the circumflex coronary artery. These electrodes were later used for recording bipolar electrograms from the future ischemic epicardium. Two additional silver electrodes were buried subcutaneously to record an electrocardiogram. The inflation tubing for the occlusive balloon and connections for the recording electrodes were externalized through skin buttons between the scapulae.

In 16 dogs a two-stage permanent coronary ligation was made on the left anterior descending artery distal to the first large diagonal branch. Of these 16 dogs, 2 died at the time of surgery because of ventricular fibrillation after the coronary artery was ligated and 3 more died within the next 72 hours of uncertain causes, possibly as a result of arrhythmia. Thus, 11 of these 16 dogs survived to be tested according to the experimental procedure described later. In six additional dogs the more distal left anterior descending artery was ligated and ligatures were placed distally on all visible branches of that vessel. None of these dogs died in the early postoperative period; however, one was sacrificed on the 11th postoperative day after it developed a refractory infection. Thus, five of these dogs went on to be tested. Myocardial infarction in the distribution of the left anterior descending artery was confirmed at subsequent postmortem examination in all dogs surviving the early postoperative course, even though two variations of surgical technique were used. All of these dogs showed a rapid ventricular tachycardia which was usually polymorphic on brief (30 seconds to a few minutes) electrocardiographic recording done 24 hours postoperatively. By the fourth or fifth postoperative day, sinus rhythm was observed without ventricular ectopic depolarizations. Although two variations of surgical technique were used to produce the anterior infarction to attempt to find the best long-term model, each dog became its own control in subsequent experiments.

Experimental procedure. Dogs were trained to stand quietly in a sling by repeated exposure to the laboratory environment. Experiments were performed between 13 and 35 days after surgery at which time all dogs seemed to have recovered from the effects of surgery. The electrocardiogram and electrograms were recorded on an Electronics for Medicine DR-12 recorder and a Hewlett-Packard 3944 magnetic recording system (used for the first two dogs). In the last six dogs recordings were made with an Electronics for Medicine VR-12 recorder and a Hewlett-Packard 3960 magnetic recording system. Constant pressure for inflating the occlusive balloon was provided from a compressed air tank through a Matheson 1-H line regulator.

Each occlusion of the circumflex coronary artery was begun approximately 45 to 60 minutes after the dog had been placed into the sling. The electrocardiogram and two sets of epicardial bipolar electrocardiograms in the circumflex distribution were recorded continuously before, during and after the occlusion. Electrograms were recorded between filter frequencies of 30 and 500 Hz at a paper speed of 100 mm/s. The occlusion was abruptly begun by turning a stopcock in the line between the compressed air tank and the tubing from the occlusive balloon. The occlusion was abruptly terminated immediately after the appearance of repetitive ventricular complexes, defined as two or more consecutive ventricular complexes, or after a maximal period of 5.5 minutes after the onset of occlusion.

Verapamil and lidocaine testing. The effect of either verapamil or lidocaine was compared with the results of preceding and subsequent control occlusions. Each of eight dogs underwent a sequence of 1) control, 2) verapamil, and 3) control experiments. Of these eight dogs, six were also tested with lidocaine at one dose or at two different doses (four were tested with two doses). Thus, there were 10 lidocaine experiments in six dogs. Sequences for these experiments are noted in Figure 1. Each dog, therefore, served as its own control.

Verapamil was given intravenously at 0.4 mg/kg body weight over 10 minutes and the occlusion was begun 10 minutes after the infusion was completed. Lidocaine was given intravenously as 1) an initial loading dose of 2 mg/kg body weight 2) a second loading dose of 1 mg/kg 20 minutes later, and 3) a maintenance infusion of 70 to 200 μg/kg per min which was started when the initial loading dose was given. Plasma lidocaine levels were drawn within 5 minutes after the occlusion was terminated while the maintenance infusion was running. Lidocaine concentrations were determined by a polarized fluorescent method (Abbott Diagnostics).

Data analysis. Observations were made on the highest grade of ventricular arrhythmia observed before release of the occlusion. The highest grade of arrhythmia observed was stratified as 1) single ventricular premature depolarizations, 2) repetitive ventricular complexes defined as two or more consecutive ventricular complexes that reverted spontaneously to sinus rhythm, and 3) ventricular fibrillation with onset before release. All but one episode of ventricular fibrillation were terminated by defibrillation with 50 to 100 J delivered by external paddles.

The latency from onset of occlusion to appearance of arrhythmia was defined as the time in seconds from the onset of occlusion until any ventricular arrhythmia appeared

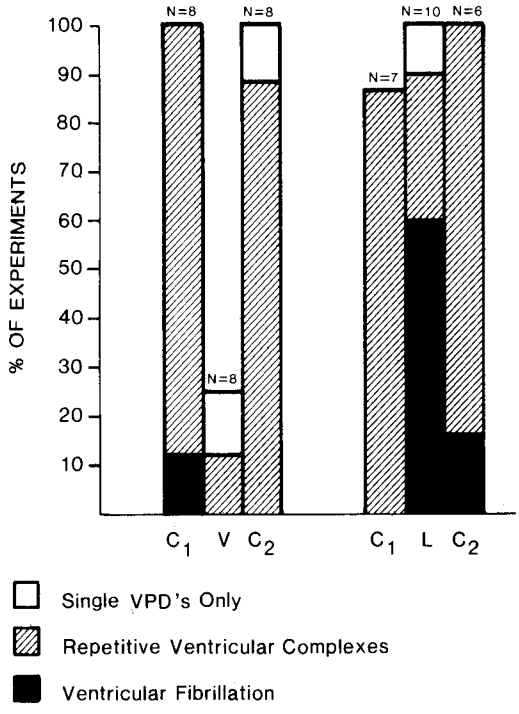


Figure 1. Incidence of the highest grade of ventricular arrhythmia observed during coronary occlusion. Each of eight dogs underwent a sequence of control (C_1), verapamil (V) and second control (C_2) experiments. Note that most dogs had no ventricular arrhythmia during verapamil occlusion. Six of these eight dogs were also tested in another sequence of control (C_1), lidocaine (L) at one dose or at two different doses and a second control (C_2) experiment. The lidocaine sequences were as follows: dog A: not tested; dog B: control, lidocaine at dose 1, lidocaine at dose 2, control; dog C: not tested; dog D: control, lidocaine at dose 1, lidocaine at dose 2 (not resuscitated); dog E: control, lidocaine at dose 1, lidocaine at dose 2, control; dog F: control, lidocaine at dose 1, control; dog G: control, lidocaine at dose 1, control; dog H: control, lidocaine at dose 1, control, lidocaine at dose 2, control. Thus, there were 7 control experiments before lidocaine administration and 10 lidocaine experiments but only 6 second control experiments because one dog had ventricular fibrillation unresponsive to attempted defibrillation during a lidocaine occlusion. VPD's = ventricular premature depolarizations.

or until release of the occlusion if no ventricular arrhythmia appeared. The effect of an intervention (that is, either verapamil or lidocaine) on latency was measured as the difference between the intervention latency and the average control latency and expressed as a percent of the average control latency.

Observations were made on the effect of verapamil and lidocaine on sinus rate before occlusion and on peak sinus rate during occlusion.

The effect of coronary occlusion on epicardial conduction delay within the ischemic zone was examined. Epicardial conduction delay was defined as the interval from the onset of the QRS of the surface electrocardiogram to the first rapid deflection of the bipolar electrogram as it crossed the baseline. The electrogram was located in the circumflex coronary artery distribution which would become ischemic during coronary occlusion. Two pairs of bipolar electrodes were arranged perpendicularly to one another on the acrylic plaque. Conduction delay was measured using each pair of electrodes. The electrode pair that demonstrated the greater change during control occlusion was used for subsequent comparisons.

The rate at which conduction delay changed with coronary occlusion was examined. The rate of change of conduction delay was not observed to be constant during serial occlusions. Therefore, to allow comparisons between control and intervention experiments, the peak conduction delay (in milliseconds) achieved during occlusion divided by the time elapsed from start of occlusion to the time at which peak delay was achieved (in seconds) was used as a measure of the rate of change for conduction delay.

Statistical analysis. Where applicable, results have been given as mean and standard error of the mean. Values obtained from the same dog were compared using paired comparison mean *t* test. Significance was established when the probability value was less than 0.05.

Results

Nine of the 16 instrumented dogs that were tested had ventricular arrhythmias on repeated control occlusions. One of these nine dogs had bradycardia and loss of consciousness during repeated control occlusions and was excluded from the data. The data were obtained from the remaining eight dogs. Of these eight, seven had the two-stage ligation of the proximal left anterior descending artery and one had ligation of the distal left anterior descending artery and its branches.

Changes in ventricular arrhythmia. The incidence of repetitive ventricular complexes during occlusion was reduced by verapamil (Fig. 1). Ventricular fibrillation during occlusion was not observed in any verapamil experiment and was only seen in one control experiment for verapamil sequences. Ventricular fibrillation during occlusion was observed in 6 of 10 lidocaine experiments as compared with only 1 of 13 control experiments (Fig. 1). Lidocaine, therefore, was associated with an increased incidence of ventricular fibrillation during occlusion.

Plasma lidocaine levels did not significantly differ in those experiments that resulted in ventricular fibrillation from those that did not (Table 1). Mean lidocaine levels were 3.8 ± 0.6 μg/ml for the entire group, 3.5 ± 0.7 μg/ml for the six experiments resulting in ventricular fibrillation and 4.2 ± 1.3 μg/ml for the four experiments without ventricular fibrillation.

Changes in latency. The mean (±SE) latency period from onset of occlusion to the appearance of the first ventricular arrhythmia for all control experiments was 116 ± 10 seconds. Thus, ventricular arrhythmias appeared very

Table 1. Effect of Lidocaine on Latency From Onset of Coronary Occlusion to Appearance of Ventricular Arrhythmia in Six Dogs

Dog	Occlusion	Lidocaine Level (μg/ml)	Latency (seconds)	Percent Change
B	Control		80	
	Lidocaine†	2.4	149	+99
	Control		70	
B	Control		80	
	Lidocaine†	4.3	77	+3
	Control		70	
D	Control		113	
	Lidocaine†	1.4	87	−23
	Control‡		—	
D	Control		113	
	Lidocaine†	2.5	65	−42
	Control‡		—	
E	Control		149	
	Lidocaine	1.2	122	+13
	Control		67	
E	Control		149	
	Lidocaine†	6.4	97	−10
	Control		67	
F	Control		117	
	Lidocaine	7.4	158	+34
	Control		119	
G	Control		330	
	Lidocaine†	4.1	30	−88
	Control		182	
H	Control		175	
	Lidocaine	4.0	203	+34
	Control		127	
H	Control		127	
	Lidocaine	4.2	131	−9
	Control		161	
Mean ± standard error				+1 ± 15.8*

*p = not significant. †Ventricular fibrillation was observed in these lidocaine experiments. ‡Control occlusion after lidocaine was not performed because the dog could not be resuscitated from ventricular fibrillation during the lidocaine occlusion (at higher dose).

early after occlusion. After verapamil administration, the latency increased significantly when compared with control in all dogs tested (Table 2). However, arrhythmias appeared in only two dogs pretreated with verapamil; arrhythmias were delayed in those two dogs and the grade of arrhythmias was also reduced. Lidocaine did not have a consistent effect on the duration of the latency period; it increased in five experiments and decreased in five experiments (Table 1).

Changes in heart rate. Sinus rate before coronary occlusion was 136 ± 12 beats/min (mean ± SE) after verapamil administration versus 120 ± 9 beats/min before verapamil and 132 ± 12 beats/min after lidocaine versus 133 ± 14 beats/min before lidocaine. These changes did not reach significance.

Peak sinus rate during occlusion was 172 ± 10 beats/min for verapamil experiments versus 187 ± 12 beats/min for control experiments and 185 ± 10 beats/min for lidocaine experiments versus 176 ± 9 beats/min for control experiments. These changes did not reach significance. In two of eight verapamil experiments second degree atrioventricular block was observed during ischemia. All other experiments demonstrated 1:1 atrioventricular conduction.

During a verapamil experiment one dog developed typical sinus tachycardia initially after the onset of occlusion; however, at 205 seconds after the start of occlusion, junctional brachycardia at a rate of 40 beats/min developed and the dog became limp and unresponsive. The dog quickly regained consciousness after release of occlusion. This same dog did not demonstrate bradycardia during control or lidocaine experiments. However, all of these occlusions were terminated sooner (in less than 205 seconds) when repetitive ventricular complexes appeared.

Change in conduction delay to the ischemic epicardium. *Verapamil.* Recordings were adequate to measure epicardial conduction delay before and during occlusion in six of eight dogs tested with verapamil, Conduction delay increased with occlusion during control experiments in five of six dogs. The mean increase in conduction delay was less during verapamil occlusion (47% increase of preocclu-

Table 2. Effect of Verapamil on Latency From Onset of Occlusion to Appearance of Ventricular Arrhythmia in Eight Dogs

Dog	Occlusion	Latency (seconds)	Percent Change
A	Control	47	
	Verapamil	115	+102
	Control	67	
B	Control	66	
	Verapamil	205	+181
	Control	80	
C	Control	90	
	Verapamil	330	+101
	Control	238	
D	Control	132	
	Verapamil	205†	+67
	Control	113	
E	Control	105	
	Verapamil	330	+160
	Control	149	
F	Control	119	
	Verapamil	330	+201
	Control	100	
G	Control	182	
	Verapamil	330	+149
	Control	83	
H	Control	144	
	Verapamil	330	+107
	Control	175	
Mean ± standard error			+ 134 ± 16.3*

*p < 0.001. †Release of occlusion was made because of apparent syncope associated with bradycardia.

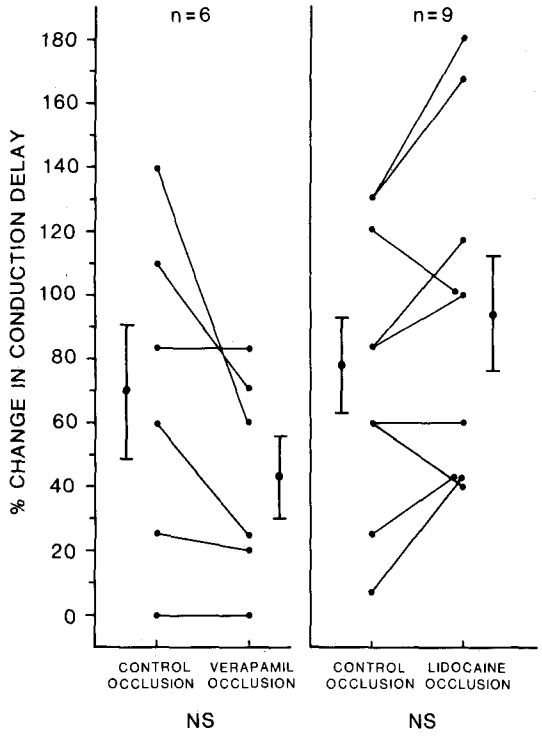


Figure 2. Effects of verapamil and lidocaine on conduction delay. The percent change from preocclusion epicardial conduction delay to the maximal conduction delay achieved during occlusion is plotted on the **ordinate**. The type of experiment is indicated on the **abscissa**. NS = not significant.

sion conduction delay) than for control experiments (70% increase); however, the difference did not reach significance (Fig. 2). All dogs demonstrating any increase in conduction delay during control occlusion showed that the rate at which conduction delay increased was retarded during verapamil occlusion as compared with control occlusion (Fig. 3). The peak conduction delay achieved during occlusion divided by the time elapsed from the start of occlusion to the appearance of peak delay was used as a measure of the rate of change in conduction delay. This value was reasonably reproducible for control experiments in a given dog, showing a strong correlation (r = 0.91) for the first two control experiments. This value was significantly less for verapamil occlusions when compared with the control (Fig. 4). That is, conduction delay into the ischemic epicardium developed sooner after the start of occlusion during control experiments than during verapamil experiments.

Lidocaine. Records were adequate to measure conduction delay in nine experiments in five dogs. Conduction delay increased for all dogs during control occlusion (Fig. 2). The mean change in conduction delay was greater for all lidocaine occlusions (94% increase of preocclusion conduction delay) than for control occlusions (78% increase). However, this did not reach significance. The rate at which conduction delay progressed after occlusion was not consistently affected by lidocaine (Fig. 4).

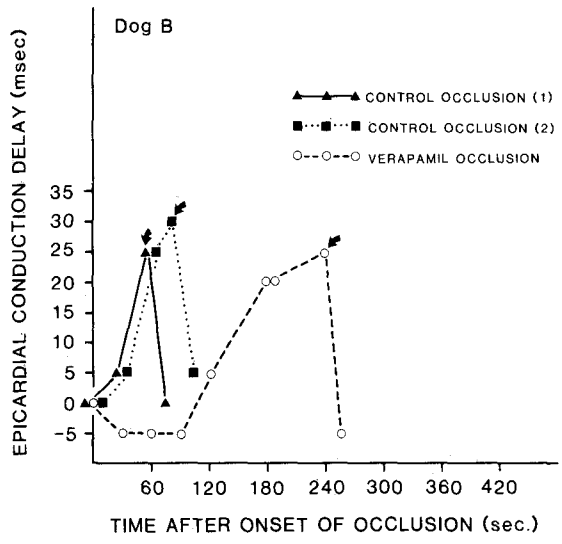
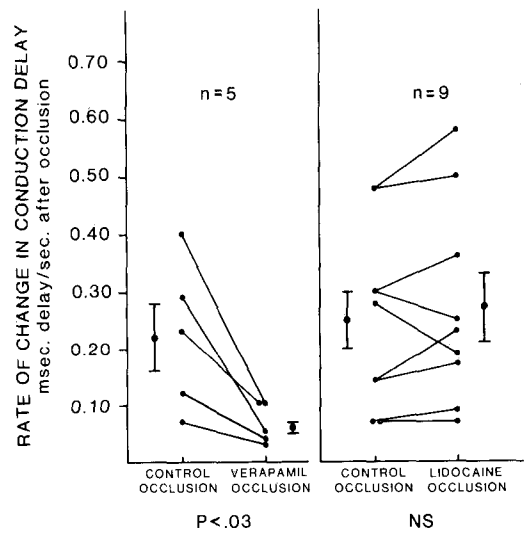


Figure 3. The relation of the increase of epicardial conduction delay **(ordinate)** and the time after the onset of coronary occlusion **(abscissa).** Note that conduction delay increases more rapidly during control occlusions compared with verapamil occlusion. Release of occlusion **(arrows)** was made when a repetitive ventricular response occurred and was followed by return of activation time toward baseline.

Discussion

Verapamil versus lidocaine. This study showed that verapamil decreased the occurrence of repetitive ventricular arrhythmias during ischemia in a conscious dog model with a previous myocardial infarction, whereas lidocaine had no

Figure 4. Effect of verapamil and lidocaine on the rate at which conduction delay changes in the ischemic epicardium after occlusion. The peak conduction delay (milliseconds) divided by the time after occlusion (seconds) at which this peak delay was first noted is plotted on the **ordinate**. The type of experiment is indicated on the **abscissa**. NS = not significant.



such beneficial effect and even showed a detrimental effect as the incidence of ventricular fibrillation was increased. When ventricular arrhythmias did occur after pretreatment with verapamil, their grade was reduced and the time from start of occlusion to their appearance was delayed. These results would suggest that verapamil had a beneficial effect in this model. These observations are significant primarily because they were made using a conscious animal model, which is more analogous to the clinical state than are the anesthetized, open chest animals used in previous studies (9–16). This model is particularly attractive because arrhythmias develop consistently after coronary occlusion and each animal may serve as its own control to identify and quantify antiarrhythmic interventions.

The model does have a potentially significant limitation: occlusions are released with the appearance of repetitive ventricular complexes or after a maximal time of 5.5 minutes and not with the appearance of ventricular fibrillation. These criteria were used so that the conscious dog would not be subjected to repeated ventricular fibrillation and so that myocardial infarction in the circumflex coronary bed would be avoided. The model appeared stable during successive control experiments. It could be argued that verapamil merely delayed the appearance of arrhythmia beyond the time of release of occlusion. However, an argument against this would be that when arrhythmias did appear with verapamil their grade was reduced. It is also possible that ventricular fibrillation might have occurred in control experiments had the occlusion not been released after the appearance of repetitive beats. But the increased incidence of ventricular fibrillation with lidocaine would suggest that a repetitive ventricular response is more likely to degenerate into ventricular fibrillation in the presence of lidocaine. Thus, lidocaine appears to facilitate ventricular fibrillation in this model.

Because the conscious dog model imposes some constraints on making electrophysiologic and hemodynamic observations, it was not within the scope of this study to determine the mechanism of the effects of verapamil or lidocaine. However, electrophysiologic observations that allow some speculations on mechanisms were made. Verapamil retarded the development of conduction delay into the ischemic epicardium. Lidocaine did not have a consistent effect on the rate at which conduction delay developed.

Previous in vivo animal studies. Conscious animal models have been used to study the effects of beta-adrenergic blocking agents in spontaneous early arrhythmias that occur during coronary occlusion. Some studies demonstrated pretreatment with beta-adrenergic blocking agents to be effective (18,19), whereas at least one different study showed propranolol to be ineffective (20).

Most investigations of other antiarrhythmic agents on ischemia-induced arrhythmias have been performed in the anesthetized open chest animal. Several authors (10–13) demonstrated that verapamil pretreatment decreases the incidence of spontaneous ventricular fibrillation within the early arrhythmic phase of coronary occlusion in the anesthetized open chest canine model. To our knowledge this has not been demonstrated previously in a conscious animal mode.

Among the antiarrhythmic agents that block fast channels, lidocaine has been investigated. The studies were done on anesthetized open chest animals and had diverse results. In a study by Borer et al. (14) the incidence of spontaneous ventricular fibrillation within 20 minutes of coronary occlusion was decreased from 88 to 45% by pretreatment with lidocaine, resulting in levels between 1.2 and 5.5 μg/ml. However, fibrillation occurred in all dogs with lidocaine levels greater than 5.5 μg/ml. Hope et al. (15) studied the effect of lidocaine on ventricular tachycardia after abrupt coronary occlusion and found that it was not protective and did not influence time of onset of arrhythmias. In their study, lidocaine levels were not reported. Spear et al. (16) studied the effect of lidocaine on the ventricular fibrillation threshold measured as the minimal current needed for a train of pulses to induce ventricular fibrillation in an anesthetized open chest dog. These investigators found that lidocaine at blood levels of 1.2 to 5.5 μg/ml reversed the decrease in fibrillation threshold accompanying acute myocardial ischemia produced within 2 minutes of coronary artery occlusion. Han et al. (17) used the response to double premature stimuli during ischemia in an anesthetized open chest dog model as a measure of antiarrhythmic efficacy. Lidocaine at blood levels of 3 to 5 μg/ml abolished single or multiple echo beats in 10 of 13 dogs. They concluded that lidocaine was effective in preventing ventricular reentrant activity during ischemia.

Verapamil: possible mechanisms of action. Although it has been theorized that a calcium channel blocker such as verapamil may be efficacious in preventing early arrhythmias by converting unidirectional block into bidirectional block and thereby abolishing reentry, this has not been demonstrated (21). Instead, previous studies (11,12,22,23) demonstrated that conduction into the ischemic epicardium improved with verapamil at a given time after occlusion. The present study extends those observations by demonstrating that verapamil improves conduction by retarding the development of conduction delay into the ischemic epicardium. Several authors (11,22) proposed that the seemingly paradoxical effects of verapamil on conduction velocity might be due to a reduction in the size of ischemic injury or degree of ischemia. In the present study, observation of verapamil retarding the development of conduction delay may reflect a slowing of the rate at which ischemia develops.

Brooks et al. (13), however, concluded that the antifibrillatory action of verapamil during coronary artery occlusion may be related, in part, to antagonism of enhanced adrenergic input into the heart. Thus, while the electro-

physiologic mechanism for the effect of verapamil on early arrhythmias remains undefined, this agent shares several significant effects with propranolol and other beta-adrenergic blocking agents: 1) beta-adrenergic blockade, 2) diminished degree of ischemia, and 3) possibly retarded rate at which ischemia develops. These may be significant antiarrhythmic effects.

Verapamil: effects on heart rate. Verapamil increased sinus rate before occlusion, although not significantly. Newman et al. (24) previously demonstrated a tachycardia after verapamil administration in the normal conscious dog with an intact autonomic nervous system. They concluded that the most probable mechanism for this increase in heart rate was the baroreceptor reflex. They hypothesized that by means of this reflex a decrease in aortic pressure, due primarily to a decrease in total peripheral resistance, resulted in reflex vagal withdrawal and increased sympathetic stimulation as well.

In the present study during coronary occlusion with verapamil pretreatment, an insignificant decrease in peak sinus heart rate was observed while second degree artrioventricular block was seen in two of eight dogs and a marked and abrupt sinus bradycardia was observed in one dog. This tendency toward decreasing sinus rate and slowing of atrioventricular conduction may have been due to the direct effect of verapamil added to the previously described vasodepressor response which occurs during ischemia of the inferoposterior left ventricle (25).

Lidocaine: possible mechanisms of action. Lidocaine has been previously demonstrated to slow conduction into ischemic myocardium while having no significant effect on conduction into the normal zone (15,22,26). It has also been demonstrated to decrease the dispersion of ventricular refractory periods between normal and ischemic myocardium in a 2 hour myocardial infarction (26). Thus, lidocaine may have antiarrhythmic effects by converting unidirectional block and reentry into bidirectional block, thus aborting reentry. The proarrhythmic effects of lidocaine in this model are unexplained. It should be noted that the present model differs from previous models in several ways: there is a previous infarction and a very large ischemic area and dogs are studied in the conscious state. It is possible that there are effects on conduction and possibly on ventricular refractoriness that were not measurable in the present model which provoked arrhythmias.

Clinical implications. In this conscious model ventricular arrhythmias are produced by ischemia in the presence of a previous myocardial infarction in a remote vascular bed. Although this model is complex it has clinical relevance because many patients with out-of-hospital cardiac arrest have had a documented previous myocardial infarction (1,3,27). Ischemia was induced between 13 and 35 days after the prior myocardial infarction in this model. This would be analogous to the first month after hospital discharge in clinical myocardial infarction. Verapamil efficacy in the present model and previous studies (10–13) suggests that long-term verapamil and possibly other agents that decrease ischemia should be tested and compared with beta-adrenergic agents in patients after myocardial infarction.

Lidocaine was administered before the onset of coronary occlusion in the present study. In the coronary care unit lidocaine is generally given after the onset of occlusion. Thus, our model is more analogous to the patient with prior myocardial infarction given a long-term fast channel blocking antiarrhythmic agent who has ischemia after hospital discharge. The effect of lidocaine in this model suggests that a prophylactically administered fast channel blocking antiarrhythmic agent may have a detrimental effect in the presence of a large area of ischemia and a previous myocardial infarction. Further investigations are needed to determine the efficacy of other fast channel blocking antiarrhythmic agents administered before the onset of ischemia in animal models with previous myocardial infarction.

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